

This is an appropriately designed study corroborating evidence for the efficacy and effectiveness of pirfenidone.

I have only some minor comments:

1) You could expand a little the introduction section, which is short i.e. i suggest you to explain the reasons for increased morbidity (the disease itself and commorbidities such as pulmonary hypertension and lung cancer). You could add a reference for these commorbidities.

I would suggest that "Karampitsakos et al Pulm Pharmacol Ther. 2018 Pulmonary hypertension in patients with interstitial lung disease."

You may also use this reference as help for improvement of the introduction section "Fletcher et al Expert Opinion on Drug Safety 2016 The safety of new drug treatments for idiopathic pulmonary fibrosis"

2) Please rephrase the phrase "Morbidity and

mortality are high, estimated 5-year survival being 20-40%" in the introduction section as there is a grammatical error.

3) introduction page 4 row 12: " an acceptable safety profile"

4) Discussion section is ver well written. I would just suggest further improving your concluding sentences by adding the words " Studies investigating effectiveness of pirfenidone in AE-IPF and studies investigating its synergistic effect with novel compounds that entered the pipeline of clinical trials (i.e. pamrevlumab, pentraxin) are greatly anticipated."

I would recommend that because data for effectiveness and safety are already known. The synergistic effect might be the hot topic of the upcoming years and if you mention that in your concluding sentences, then you enhance future perspectives of your manuscript. Towards this direction, you could add these 3 references in your concluding sentences.

1) Karampitsakos et al Front Med 2019 Biologic Treatments in Interstitial Lung Diseases

2) Raghu et al JAMA 2018 Effect of Recombinant Human Pentraxin 2 vs Placebo on Change in Forced Vital Capacity in Patients With Idiopathic Pulmonary Fibrosis: A Randomized Clinical Trial.

3) Richeldi et al Lancet RM 2019 Pamrevlumab, an anti-connective tissue growth factor therapy, for idiopathic pulmonary fibrosis (PRAISE): a phase 2, randomised, double-blind, placebo-controlled trial.